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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/441,313	11/16/1999	ALLAN SVENDSEN	5709.200-US	4161

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EXAMINER	
HUTSON, RICHARD G	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 08/09/2002 16

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/441,313	SVENDSEN ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *42-61* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *42,44-48,51,52,55-58,60 and 61* is/are rejected.

7)☒ Claim(s) *43,49,50 and 59* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicants amendment of the specification, cancellation of claims 1-18, 24, 27, 29, 31 and 41 without prejudice and the addition of new claims 42-61, Paper No. 12, is acknowledged. Claims 42-61 are at issue and are present for examination.

Applicants' arguments filed on 1/24/2002, paper No. 12, have been fully considered and are deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Objections

Claims 43, 49, 50, 53 and 59 are objected to because of the following informalities: Claims 43 and 53 depend from rejected claims.

Appropriate correction is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 42 and 44-48 are rejected under 35 U.S.C. 102(b) as being anticipated by Nielson et al. (U.S. Patent No: 5,731,280, March 1998).

Nielson et al. teach a recombinant *Bacillus lichenformis* alpha-amylase Y358 mutant having at least 95% identity to SEQ ID NO: 4 and a DNA encoding said variant alpha-amylase.

Thus, Nielson et al. anticipates claims 42 and 44-48 drawn to a DNA sequence encoding an alpha-amylase having at least 95% amino acid identity to SEQ ID NO: 4 and having an alteration at Y358.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 54-58, 60 and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Svendsen et al. (WO 96/23874, 1996).

Svendsen et al. (1996) was relied upon in the previous 102 rejection of now cancelled claim 18.

Svendsen et al. (1996) teach methods of constructing and variants of a parent Termamyl-like α-amylase wherein the variant has α-amylase activity and at least one altered property as compared to the parent α-amylase. The parent Termamyl-like α-amylases include and/or are derived from a strain of *B. licheniformis, B. amyloliquefaciens, B. stearothermopnilus, Bacillus* sp. NCIB 12289, NCIB 12512, NCIB 12513 or DSM 9375, as well as the *B. licheniformis* ATCC 27811 (page 5, lines 20-page

6 line 8 and pages 7-8). The parent Termamyl-like α-amylase may also include hybrids of the *B. licheniformis* α-amylase and *B. amyloliquefaciens* α–amylase. These parent alpha-amylases include those which are at least 95% identical to Sinstantly disclosed SEQ ID NO: 4. The properties of the variant that are altered relative to the parent enzyme include calcium dependency, substrate binding, cleavage pattern, pH dependent activity and the like. Specifically, Svendsen et al. (1996) teach a variant which has been modified in one or more amino acid residues present within 10A of the calcium binding site of the *B. licheniformis* α-amylase. These residues include but are not limited to K176, A181, I201, H205, A209, **S417** and **A420** (page 30, line 11). Mutations which lead to increased calcium stability and/or thermostability of the enzyme may be achieved by introduction of residues which increase the hydrophobic interactions (page 33, lines 6-8). Svendsen et al. (1996) teach a number of variants which reduce calcium dependency including the following: R23K, H156Y, A181T, A209V and G310D or the equivalent mutations in equivalent positions in another Termamyl-like α-amylase (page 33, lines 33-38). Svendsen et al. (1996) further teach variants with increased thermostability and/or altered temperature optimum. These variants are created by reducing the number of holes and crevices found in the parent Termamyl-like α-amylase with residues that introduce more hydrophobic contacts, preferably achieved by introducing bulkier residues, in the vicinity of the hole (page 36, lines 26-36). Svendsen et al. (1996) further teach the use of said variant α-amylases in detergent additives and compositions, manual or automatic dishwashing detergent

compositions and manual or automatic laundry washing compositions (page 59-page 71).

Svendsen et al. (1996) also teach DNA constructs encoding the above variants, as well as vectors comprising said DNA constructs and host cells comprising said vectors and DNA constructs.

One of ordinary skill in the art at the time of filing would have been motivated to create DNAs encoding variant alpha amylases in which those residues which reduce the Ca^{2+} dependency of the enzyme, so that the variant can be used at lower Ca^{2+} concentrations such as the conditions of certain detergents. Specifically two of the residues involved in such Ca^{2+} binding are identified by Svendsen et al. who teach the mutation of S417 or A420 and teach that those mutant residues that introduce more hydrophobic contacts, preferably achieved by introducing bulkier residues, in the vicinity of the hole are desirable, such as S417T or A420Q or R. The choice of these specific residues is a result of the increased bulkiness of threonine vs serine and glutamine or arginine versus alanine. Thus the DNA encoding the variant alpha amylase comprising S417T or A420 Q or R is obvious over the teachings of Svendsen et al. The reasonable expectation of success comes from the high degree of knowledge in the art with respect to alpha-amylases, DNAs and their mutation and the results of Svendsen et al. who teach specifically many additional mutations of a number of alpha-amylases.

Therefore, Svendsen et al. (1996) make obvious claims 54-58, 60 and 61.

Claims 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nielson et al. (U.S. Patent No: 5,731,280, March 1998) and Svendsen et al. (WO 97/41213, 1997).

As discussed above, Nielson et al. teach a recombinant *Bacillus lichenformis* alpha-amylase Y358 mutant and a DNA encoding said variant alpha-amylase.

Svendsen et al. (1997) teach variants of a parent Termamyl-like α-amylase. The parent α-amylase may comprise a C-terminal part of an α-amylase derived from a strain of *B. licheniformis* and a N-terminal part of an α-amylase derived from a strain of *B. amyloliquefaciens* (page 5-6). Specifically, Svendsen et al. (1997) teach a variant having an altered property such as increased stability at low pH and low Ca^+ concentration and comprising the mutation H156Y+A181T+N190F+A209V+Q264S (page 88, claim 2), designated in the instant disclosure as "LE174". Svendsen et al. (1997) further teach the use of the above variant as a parent Termamyl-like α-amylase that is further mutated by random mutagenesis (Examples 1 and 2). Svendsen et al. (1997) teach a variant having an altered property such as increased stability at low pH and low Ca^+ concentration and comprising the mutation H156Y+A181T+N190F+A209V+Q264S (page 88, claim 2), that further has a mutation at H205C (page 62, lines 25-28).

As discussed above, Svendsen et al. (1997) teach variants of a parent Termamyl-like α-amylase. The parent α-amylase may comprise a C-terminal part of an α-amylase derived from a strain of *B. licheniformis* and a N-terminal part of an α-amylase derived from a strain of *B. amyloliquefaciens* (page 5-6). One of ordinary skill

in the art at the time of filing would have been motivated to combine the mutations taught by Nielson et al., specifically Y 358 and those of Svendsen et al. (1997), specifically, H156Y+A181T+N190F+A209V+Q264S and H205C in order to create a DNA that encodes a variant alpha amylase which is more stable at low pH and low Ca^{+} concentration then either parent alpha-amylase. As discussed above, the reasonable expectation of success comes from the high degree of knowledge in the art with respect to alpha-amylases, the DNAs which encode them and their mutation and the results of both Nielson et al. and Svendsen et al. who specifically teach many additional mutations of a number of alpha-amylases.

Therefore, Nielson et al. and Svendsen et al. (1997) make obvious claims 51 and 52.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

REBECCA E. PROUTY
PRIMARY EXAMINER
GROUP ~~1800~~ 1600

Richard Hutson, Ph.D.
Patent Examiner
Art Unit 1652
August 8, 2002